

Table S1. List of phytochemicals and their canonical SMILES used in this study.

| S. No | Compound Name | Abbreviation | Canonical SMILES |
|-------|----------------------|--------------|--|
| 1 | Berberine | BER | <chem>COC1=C(C2=C[N+]3=C(C=C2C=C1)C4=CC5=C(C=C4CC3)OCO5)OC</chem> |
| 2 | Palmatine | PAL | <chem>COC1=C(C2=C[N+]3=C(C=C2C=C1)C4=CC(=C(C=C4CC3)OC)OC)OC</chem> |
| 3 | Coptisine | COP | <chem>C1C[N+]2=C(C=C3C=CC4=C(C3=C2)OCO4)C5=CC6=C(C=C51)OCO6</chem> |
| 4 | Atractylenolide I | ATA | <chem>CC1=C2CC3C(=C)CCCC3(C=C2OC1=O)C</chem> |
| 5 | Taraxeryl acetate | TAR | <chem>CC(=O)OC1CCC2(C(C1(C)C)CCC3(C2CCC4(C3=CCC5(C4CC(CC5)(C)C)C)C)C)C</chem> |
| 6 | Lupeol | LUP | <chem>CC(=C)C1CCC2(C1C3CCC4C5(CCC(C(C5CCC4(C3(CC2)C)C)(C)C)O)C)C</chem> |
| 7 | Ginsenosides | GSN | <chem>CC(=CCCC(C)(C1CCC2(C1CCC3C2(CCC4C3(CCC(C4(C)C)O)C)C)O)C</chem> |
| 8 | Ginseng Tetrapeptide | GST | <chem>CC(C)C(C(=O)NC(CCC(=O)NC(CCCN=C(N)N)C(=O)NCC(=O)O)C(=O)O)N</chem> |
| 9 | Lotusine B | LTB | <chem>CCC(C)C1C(=O)NC=CC2=CC=C(C=C2)OC3CCN(C3C(=O)N1)C(=O)C(CC4=CC=CC=C4)NC(=O)C(CC(C)C)N(C)C</chem> |
| 10 | Jujubogenin | JJG | <chem>CC(=CC1CC(C2C3CCC4C5(CCC(C(C5CCC4(C36CC2(O1)OC6)C)(C)C)O)C)(C)O)C</chem> |
| 11 | Jujuboside A | JJA | <chem>CC1C(C(C(C(O1)OC2C(C(COC2OC3CCC4(C5CCC6C7C(CC(OC78CC6(C5(CCC4C3(C)C)C)CO8)C=C(C)C)(C)O)C)O)OC9C(C(C(C(O9)COC1C(C(C(C(O1)CO)O)O)O)O)OC1C(C(C(CO1)O)O)O)O)O</chem> |
| 12 | Coixenolide | CXL | <chem>CCCCCCC=CCCCCCCCCCCC(=O)OC(C)C(C)OC(=O)CCCCCCCC=CCCCCCC</chem> |
| 13 | Betasitosterol | BST | <chem>CCC(CCC(C)C1CCC2C1(CCC3C2CC=C4C3(CCC(C4)O)C)C(C)C</chem> |
| 14 | Caffeic acid | CFA | <chem>C1=CC(=C(C=C1C=CC(=O)O)O)O</chem> |
| 15 | Naringenin | NGN | <chem>C1C(OC2=CC(=CC(=C2C1=O)O)O)C3=CC=C(C=C3)O</chem> |
| 16 | Trigonelline | TGL | <chem>C[N+]1=CC=CC(=C1)C(=O)[O-]</chem> |
| 17 | Gentianine | GTN | <chem>C=CC1=CN=CC2=C1CCOC2=O</chem> |
| 18 | Quercetin | QRC | <chem>C1=CC(=C(C=C1C2=C(C(=O)C3=C(C=C(C=C3O2)O)O)O)O</chem> |
| 19 | Gallic acid | GLA | <chem>C1=C(C=C(C(=C1O)O)O)C(=O)O</chem> |
| 20 | Epicatechin gallate | ECG | <chem>C1C(C(OC2=CC(=CC(=C21)O)O)C3=CC(=C(C=C3)O)O)OC(=O)C4=CC(=C(C(=C4)O)O)O</chem> |

| | | | |
|----|--------------------------|-----|---|
| 21 | Kaempferol | KPF | <chem>C1=CC(=CC=C1C2=C(C(=O)C3=C(C=C(C(=C3O2)O)O)O)O</chem> |
| 22 | 6-Gingerol | GGL | <chem>CCCCC(CC(=O)CCC1=CC(=C(C=C1)O)OC)O</chem> |
| 23 | Zingerone | ZGN | <chem>CC(=O)CCC1=CC(=C(C=C1)O)OC</chem> |
| 24 | Citral | CTL | <chem>CC(=CCCC(=CC=O)C)C</chem> |
| 25 | Beta-Amyrin | BMR | <chem>CC1(CCC2(CCC3(C(=CCC4C3(CCC5C4(CCC(C5(C)C)O)C)C)C2C1)C)C)C</chem> |
| 26 | 7,8-dimethoxycoumarin | DMC | <chem>COC1=C(C2=C(C=C1)C=CC(=O)O2)OC</chem> |
| 27 | Xanthosin | XNS | <chem>CC1CC2C(CC=C1CCC(=O)C)C(=C)C(=O)O2</chem> |
| 28 | Xanthanol | XNL | <chem>C1=CC=C2C(=C1)C(C3=CC=CC=C3O2)O</chem> |
| 29 | Apigetrin | AGT | <chem>C1=CC(=CC=C1C2=CC(=O)C3=C(C=C(C(=C3O2)OC4C(C(C(C(O4)CO)O)O)O)O)O</chem> |
| 30 | Astragaloside | AGS | <chem>COC1=C(C=CC(=C1)C2=C(C(=O)C3=C(C=C(C(=C3O2)O)O)OC4C(C(C(C(O4)COC5C(C(C(C(O5)CO)O)O)O)O)O)O)O</chem> |
| 31 | Chlorogenic acid | CGA | <chem>C1C(C(C(CC1(C(=O)O)O)OC(=O)C=CC2=CC(=C(C=C2)O)O)O)O</chem> |
| 32 | Kaemferol-3-O-rutinoside | KFR | <chem>CC1C(C(C(C(O1)OCC2C(C(C(C(O2)OC3=C(OC4=CC(=CC(=C4C3=O)O)O)C5=CC=C(C=C5)O)O)O)O)O)O</chem> |
| 33 | Carthamin | CRN | <chem>C1=CC(=CC=C1C=CC(=O)C2=C(C(C(=C(C2=O)C=C3C(=O)C(=C(C(C3=O)(C4C(C(C(C(O4)CO)O)O)O)O)O)C(=O)C=CC5=CC=C(C=C5)O)O)(C6C(C(C(C(O6)CO)O)O)O)O)O)O</chem> |
| 34 | Hydroxysafflor yellow A | HYA | <chem>C1=CC(=CC=C1C=CC(=C2C(=C(C(=O)C(C2=O)(C3C(C(C(C(O3)CO)O)O)O)O)C4C(C(C(C(O4)CO)O)O)O)O)O</chem> |

Table S2. KEGG pathway enrichment analysis of unique genes and their involvement in CAC-related metabolic pathways.

| Pathway.ID | Pathway Description | p.Val | FDR | Genes |
|------------|---|-------------|-------------|--|
| KEGG:05417 | Lipid and atherosclerosis | 5.04E-10 | 5.04E-10 | IKBKB,STAT3,MMP9,PPARG,GSK3B,NLRP3,TLR4,RELA,TNF,EIF2AK3,TP53,SELP |
| KEGG:04210 | Apoptosis | 1.85735E-06 | 1.85735E-06 | IKBKB,CAPN1,BIRC3,MAP3K14,RELA,TNF,EIF2AK3,TP53 |
| KEGG:05142 | Chagas disease | 5.29392E-06 | 5.29392E-06 | IKBKB,NOS2,ACE,TLR4,RELA,SERPINE1,TNF |
| KEGG:05171 | Coronavirus disease - COVID-19 | 8.32947E-06 | 8.32947E-06 | IKBKB,STAT3,F2,ACE,NLRP3,TLR4,RELA,TNF,SELP |
| KEGG:05145 | Toxoplasmosis | 8.98276E-06 | 8.98276E-06 | IKBKB,STAT3,NOS2,BIRC3,TLR4,RELA,TNF |
| KEGG:05162 | Measles | 4.75766E-05 | 4.75766E-05 | IKBKB,STAT3,GSK3B,TLR4,RELA,EIF2AK3,TP53 |
| KEGG:04936 | Alcoholic liver disease | 5.49983E-05 | 5.49983E-05 | IKBKB,GSK3B,SIRT1,MAP3K14,TLR4,RELA,TNF |
| KEGG:05160 | Hepatitis C | 0.00010839 | 0.00010839 | IKBKB,STAT3,GSK3B,RELA,TNF,EIF2AK3,TP53 |
| KEGG:05161 | Hepatitis B | 0.000128361 | 0.000128361 | IKBKB,STAT3,MMP9,TLR4,RELA,TNF,TP53 |
| KEGG:04064 | NF-kappa B signaling pathway | 0.000133846 | 0.000133846 | IKBKB,BIRC3,MAP3K14,TLR4,RELA,TNF |
| KEGG:05131 | Shigellosis | 0.000187411 | 0.000187411 | IKBKB,GSK3B,CAPN1,NLRP3,TLR4,RELA,TNF,TP53 |
| KEGG:04668 | TNF signaling pathway | 0.000243938 | 0.000243938 | IKBKB,MMP9,BIRC3,MAP3K14,RELA,TNF |
| KEGG:05202 | Transcriptional misregulation in cancer | 0.000414985 | 0.000414985 | MMP9,PPARG,BIRC3,NGFR,RELA,IGFBP3,TP53 |
| KEGG:05130 | Pathogenic Escherichia coli infection | 0.000475524 | 0.000475524 | IKBKB,TUBB3,F2,NLRP3,TLR4,RELA,TNF |
| KEGG:05133 | Pertussis | 0.000614228 | 0.000614228 | NOS2,NLRP3,TLR4,RELA,TNF |
| KEGG:05135 | Yersinia infection | 0.000713926 | 0.000713926 | IKBKB,GSK3B,NLRP3,TLR4,RELA,TNF |
| KEGG:05200 | Pathways in cancer | 0.001097739 | 0.001097739 | IKBKB,STAT3,MMP9,PPARG,F2,NOS2,GSK3B,BIRC3,RELA,TP53 |
| KEGG:04932 | Non-alcoholic fatty liver disease | 0.001454047 | 0.001454047 | IKBKB,PPARG,GSK3B,RELA,TNF,EIF2AK3 |
| KEGG:04657 | IL-17 signaling pathway | 0.001485521 | 0.001485521 | IKBKB,MMP9,GSK3B,RELA,TNF |
| KEGG:04218 | Cellular senescence | 0.001564786 | 0.001564786 | CAPN1,SIRT1,RELA,SERPINE1,IGFBP3,TP53 |
| KEGG:05222 | Small cell lung cancer | 0.001566713 | 0.001566713 | IKBKB,NOS2,BIRC3,RELA,TP53 |
| KEGG:04217 | Necroptosis | 0.001743585 | 0.001743585 | STAT3,CAPN1,BIRC3,NLRP3,TLR4,TNF |
| KEGG:05215 | Prostate cancer | 0.002025969 | 0.002025969 | IKBKB,MMP9,GSK3B,RELA,TP53 |
| KEGG:05132 | Salmonella infection | 0.002262994 | 0.002262994 | IKBKB,TUBB3,BIRC3,NLRP3,TLR4,RELA,TNF |
| KEGG:05164 | Influenza A | 0.002381209 | 0.002381209 | IKBKB,NLRP3,TLR4,RELA,TNF,PLG |
| KEGG:04660 | T cell receptor signaling pathway | 0.002708325 | 0.002708325 | IKBKB,GSK3B,MAP3K14,RELA,TNF |

| | | | | |
|------------|--|-------------|-------------|---|
| KEGG:04625 | C-type lectin receptor signaling pathway | 0.002837532 | 0.002837532 | IKBKB,MAP3K14,NLRP3,RELA,TNF |
| KEGG:04931 | Insulin resistance | 0.003402919 | 0.003402919 | IKBKB,STAT3,GSK3B,RELA,TNF |
| KEGG:04066 | HIF-1 signaling pathway | 0.003557021 | 0.003557021 | STAT3,NOS2,TLR4,RELA,SERPINE1 |
| KEGG:04621 | NOD-like receptor signaling pathway | 0.003734966 | 0.003734966 | IKBKB,BIRC3,NLRP3,TLR4,RELA,TNF |
| KEGG:05010 | Alzheimer disease | 0.004654905 | 0.004654905 | IKBKB,TUBB3,NOS2,GSK3B,CAPN1,RELA,TNF,EIF2AK3 |
| KEGG:04722 | Neurotrophin signaling pathway | 0.005200676 | 0.005200676 | IKBKB,GSK3B,NGFR,RELA,TP53 |
| KEGG:05321 | Inflammatory bowel disease | 0.005804451 | 0.005804451 | STAT3,TLR4,RELA,TNF |
| KEGG:05169 | Epstein-Barr virus infection | 0.005975193 | 0.005975193 | IKBKB,STAT3,MAP3K14,RELA,TNF,TP53 |
| KEGG:04380 | Osteoclast differentiation | 0.006842309 | 0.006842309 | IKBKB,PPARG,MAP3K14,RELA,TNF |
| KEGG:04920 | Adipocytokine signaling pathway | 0.008829943 | 0.008829943 | IKBKB,STAT3,RELA,TNF |
| KEGG:05140 | Leishmaniasis | 0.010424787 | 0.010424787 | NOS2,TLR4,RELA,TNF |
| KEGG:05418 | Fluid shear stress and atherosclerosis | 0.010922754 | 0.010922754 | IKBKB,MMP9,RELA,TNF,TP53 |
| KEGG:05163 | Human cytomegalovirus infection | 0.011510504 | 0.011510504 | IKBKB,STAT3,GSK3B,RELA,TNF,TP53 |
| KEGG:05212 | Pancreatic cancer | 0.012863415 | 0.012863415 | IKBKB,STAT3,RELA,TP53 |
| KEGG:01523 | Antifolate resistance | 0.013389849 | 0.013389849 | IKBKB,RELA,TNF |
| KEGG:04211 | Longevity regulating pathway | 0.023651662 | 0.023651662 | PPARG,SIRT1,RELA,TP53 |
| KEGG:05235 | PD-L1 expression and PD-1 checkpoint pathway in cancer | 0.023651662 | 0.023651662 | IKBKB,STAT3,TLR4,RELA |
| KEGG:04933 | AGE-RAGE signaling pathway in diabetic complications | 0.036893696 | 0.036893696 | STAT3,RELA,SERPINE1,TNF |
| KEGG:05146 | Amoebiasis | 0.038313492 | 0.038313492 | NOS2,TLR4,RELA,TNF |
| KEGG:04620 | Toll-like receptor signaling pathway | 0.03977185 | 0.03977185 | IKBKB,TLR4,RELA,TNF |
| KEGG:04062 | Chemokine signaling pathway | 0.047993483 | 0.047993483 | IKBKB,STAT3,CCR2,GSK3B,RELA |

Table S3. List of cachexia-related genes used in this study.

| S. No | Gene | Reference |
|-------|---------|----------------------|
| 1 | mTORC1 | Setiawan et al. 2023 |
| 2 | mTORC2 | |
| 3 | MYOD1 | |
| 4 | UCP1 | |
| 5 | IGF1 | |
| 6 | AKT | |
| 7 | JUP | |
| 8 | BMP | |
| 9 | BMP7 | |
| 10 | MSTN | |
| 11 | ACVR1 | |
| 12 | SMAD2 | |
| 13 | SMAD3 | |
| 14 | NFKB1 | |
| 15 | MAP3K14 | |
| 16 | TNF | |
| 17 | STAT3 | |
| 18 | IL6 | |
| 19 | BNIP3 | |
| 20 | LC3B | |
| 21 | FOXO3 | |
| 22 | ATG7 | |
| 23 | PI3K | |
| 24 | CAPN1 | |
| 25 | KCTD7 | |
| 26 | PIF | |

| | | |
|----|-----------|------------------------|
| 27 | TRIM63 | Narasimhan et al. 2021 |
| 28 | SLC39A4 | |
| 29 | PDK4 | |
| 30 | SDF1 | |
| 31 | CEBPA | |
| 32 | CXCR4 | |
| 33 | EIF2AK3 | |
| 34 | COL1A1 | |
| 35 | HMGCS2 | |
| 36 | COL3A1 | |
| 37 | ASPN | |
| 38 | DDN | |
| 39 | TMEM8C | |
| 40 | CHI3L1 | |
| 41 | LOC653513 | |
| 42 | MXRA5 | |
| 43 | SAA2 | |
| 44 | THY1 | |
| 45 | CPXM1 | |
| 46 | HP | |
| 47 | SFRP4 | |
| 48 | SLC5A1 | |
| 49 | MMP9 | |
| 50 | TYRP1 | |
| 51 | NOV | |
| 52 | COL1A2 | |
| 53 | ECEL1 | |
| 54 | KRT80 | |
| 55 | CCL19 | |

| | |
|----|----------|
| 56 | COL5A1 |
| 57 | SFRP2 |
| 58 | SERPINE1 |
| 59 | FZD10 |
| 60 | GLT1D1 |
| 61 | CRABP2 |
| 62 | STMN2 |
| 63 | CCL3 |
| 64 | TPPP3 |
| 65 | TMEM119 |
| 66 | LUM |
| 67 | FXYP4 |
| 68 | SPON1 |
| 69 | TNC |
| 70 | ELN |
| 71 | SLAMF8 |
| 72 | CILP2 |
| 73 | CCL13 |
| 74 | CCDC80 |
| 75 | OGN |
| 76 | MOXD1 |
| 77 | CD69 |
| 78 | ERBB3 |
| 79 | LGI2 |
| 80 | IGJ |
| 81 | CAMSAP3 |
| 82 | CKB |
| 83 | COL5A2 |
| 84 | MSMP |

| | |
|-----|----------|
| 85 | TTC39A |
| 86 | MGC39372 |
| 87 | C2 |
| 88 | CD163L1 |
| 89 | ZNF556 |
| 90 | CELSR1 |
| 91 | BHLHE22 |
| 92 | MYH3 |
| 93 | CTHRC1 |
| 94 | TUBB3 |
| 95 | KAZALD1 |
| 96 | IGLL5 |
| 97 | ESM1 |
| 98 | MYBPH |
| 99 | COL14A1 |
| 100 | TNFAIP6 |
| 101 | FAIM2 |
| 102 | PHOSPHO1 |
| 103 | VASH2 |
| 104 | SMIM5 |
| 105 | CH25H |
| 106 | GDF10 |
| 107 | CERCAM |
| 108 | FNDC1 |
| 109 | CD200R1 |
| 110 | CYS1 |
| 111 | SHANK1 |
| 112 | MYL5 |
| 113 | CRISPLD1 |

| | |
|-----|----------|
| 114 | FAM180B |
| 115 | CRMP1 |
| 116 | PDE6G |
| 117 | LTK |
| 118 | GADD45G |
| 119 | ABLIM1 |
| 120 | TNFRSF18 |
| 121 | NLRP3 |
| 122 | ARHGDIG |
| 123 | CASKIN1 |
| 124 | IGSF10 |
| 125 | SIGLEC9 |
| 126 | THBS4 |
| 127 | ADAMTS2 |
| 128 | EMB |
| 129 | RASD1 |
| 130 | MMP11 |
| 131 | LBP |
| 132 | ITGB8 |
| 133 | LRRC17 |
| 134 | FPR3 |
| 135 | NGFR |
| 136 | PRG4 |
| 137 | CCR2 |
| 138 | INHBE |
| 139 | ABCC6 |
| 140 | SLC45A3 |
| 141 | OXCT2 |
| 142 | FZD2 |

| | |
|-----|------------|
| 143 | FAM57B |
| 144 | IL4I1 |
| 145 | IL7R |
| 146 | CCL4 |
| 147 | HSD11B2 |
| 148 | RHOH |
| 149 | TNFAIP8L3 |
| 150 | PMAIP1 |
| 151 | LILRB4 |
| 152 | PNMA2 |
| 153 | PITPNM1 |
| 154 | KDEL3 |
| 155 | GPR183 |
| 156 | DIO2 |
| 157 | TMEM59L |
| 158 | CCL2 |
| 159 | GNA15 |
| 160 | SOX3 |
| 161 | CILP |
| 162 | BRSK1 |
| 163 | PRUNE2 |
| 164 | QPCT |
| 165 | CYP4F11 |
| 166 | IFITM10 |
| 167 | CERKL |
| 168 | ST6GALNAC2 |
| 169 | FOXI2 |
| 170 | BICD1 |
| 171 | ASPHD2 |

| | | |
|-----|---------|-----------------|
| 172 | ABO | |
| 173 | SVOP | |
| 174 | OSM | |
| 175 | VCAN | |
| 176 | OMD | |
| 177 | SOCS3 | |
| 178 | TNFRSF9 | |
| 179 | MYLK | |
| 180 | PAPLN | |
| 181 | VIPR2 | |
| 182 | ITGA11 | |
| 183 | SELP | Tan et al. 2011 |
| 184 | LTA | |
| 185 | IL-1B | |
| 186 | ACE | |
| 187 | LPL | |
| 188 | RETN | |
| 189 | ADIPOQ | |
| 190 | Akt | |
| 192 | Ap1 | |
| 193 | ERK1 | |
| 194 | ERK2 | |
| 195 | IFNG | |
| 196 | IGFBP3 | |
| 197 | IgG | |
| 198 | IL12 | |
| 199 | LDL | |
| 200 | LEP | |
| 201 | Mapk | |

| | |
|-----|--------|
| 202 | NFkB |
| 204 | MAPK |
| 205 | PDGFB |
| 206 | PPARG |
| 207 | Sod |
| 208 | TLR2 |
| 209 | TLR4 |
| 210 | Vegf |
| 211 | ADRB2 |
| 212 | BIRC3 |
| 213 | BTG2 |
| 214 | CAMP |
| 215 | CREBBP |
| 216 | CRP |
| 217 | CSF1 |
| 218 | F2 |
| 219 | GSK3B |
| 220 | HDAC3 |
| 221 | HGF |
| 222 | HMGB1 |
| 223 | HSPD1 |
| 224 | IKBKB |
| 225 | IL17A |
| 226 | IL6R |
| 227 | IRS1 |
| 228 | LTF |
| 229 | NFIC |
| 230 | NOS2 |
| 231 | NR3C1 |

| | | |
|-----|---------|--|
| 232 | PLD1 | |
| 233 | PLG | |
| 234 | RELA | |
| 235 | SIRT1 | |
| 236 | TNFSF12 | |
| 237 | TP53 | |
| 238 | TSC22D3 | |